

# *STN Search History*

FILE 'HOME' ENTERED AT 11:52:18 ON 11 SEP 2003

L1 QUE (MOUSE OR MURINE OR MICE) (P) (FUSIN OR CXCR-4 OR CXCR4 OR CXCR ADJ 4)

L3 420 L2 AND (POLYNUCLEOTIDE OR DNA OR !DNA OR NUCLEIC OR GENE) (P)  
(FUSIN OR CXCR-4 OR CXCR4 OR CXCR ADJ 4)

L14 1266 (MOUSE OR MURINE OR MICE) (P) (FUSIN OR CXCR-4 OR CXCR4 OR CXCR  
ADJ 4)

(FILE 'HOME' ENTERED AT 11:52:18 ON 11 SEP 2003)

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,  
BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,  
CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB,  
DDFU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, ...' ENTERED AT 11:52:35 ON  
11 SEP 2003

SEA (MOUSE OR MURINE OR MICE) (P) (FUSIN OR CXCR-4 OR CXCR4 OR

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5 FILE ADISINSIGHT  
2\* FILE ADISNEWS  
1 FILE AGRICOLA  
1 FILE AQUASCI  
3 FILE BIOBUSINESS  
0\* FILE BIOCOMMERCE  
283 FILE BIOSIS  
22\* FILE BIOTECHABS  
22\* FILE BIOTECHDS  
207\* FILE BIOTECHNO  
3 FILE CABA  
111 FILE CANCERLIT  
231 FILE CAPLUS  
1\* FILE CEABA-VTB  
1 FILE CEN  
3\* FILE CIN  
6 FILE CONFSCI  
27 FILE DDFU  
20 FILE DGENE  
41 FILE DRUGU  
2 FILE DRUGUPDATES  
14 FILE EMBAL  
191 FILE EMBASE  
176\* FILE ESBIOSBASE  
56\* FILE FEDRIP  
0\* FILE FOMAD  
0\* FILE FOREGE  
0\* FILE FROSTI  
0\* FILE FSTA  
44 FILE GENBANK  
38 FILE IFIPAT  
11 FILE JICST-EPLUS  
0\* FILE KOSMET  
134 FILE LIFESCI  
0\* FILE MEDICONF  
220 FILE MEDLINE  
0\* FILE NTIS  
0\* FILE NUTRACEUT  
53\* FILE PASCAL

4 FILE PHAR  
1\* FILE PHARMAML  
18 FILE PROMT  
280 FILE SCISEARCH  
90 FILE TOXCENTER  
120 FILE USPATFULL  
5 FILE USPAT2  
24 FILE WPIDS  
24 FILE WPINDEX  
L1 QUE (MOUSE OR MURINE OR MICE) (P) (FUSIN OR CXCR-4 OR CXCR4 OR  
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FILE 'MEDLINE, CAPLUS, BIOSIS, BIOTECHNO, LIFESCI, EMBASE, SCISEARCH'  
ENTERED AT 11:55:15 ON 11 SEP 2003

L2 1546 S L1  
L3 420 S L2 AND (POLYNUCLEOTIDE OR DNA OR !DNA OR NUCLEIC OR GENE) (P)  
L4 149 S L3 AND (CD4 OR HCD4 OR T4) (P) (RECEPTOR OR CO-RECEPTOR)  
L5 55 DUP REM L4 (94 DUPLICATES REMOVED)  
L6 14 S L5 NOT PY>1997  
L7 33 S L3 AND MURINE (4N) (FUSIN OR CXCR-4 OR CXCR4 OR CXCR ADJ 4)  
L8 12 DUP REM L7 (21 DUPLICATES REMOVED)  
L9 3 S L8 AND L6  
L10 20 S (L6 OR L8) NOT L9  
L11 20 DUP REM L10 (0 DUPLICATES REMOVED)  
L12 68765 S (MURINE OR MOUSE) (S) (CD4 OR HCD4)  
L13 1546 S L1 AND (FUSIN OR CXCR-4 OR CXCR4 OR CXCR ADJ 4)  
L14 1266 S (MOUSE OR MURINE OR MICE) (P) (FUSIN OR CXCR-4 OR CXCR4 OR CX  
L15 1546 S L13 AND L2  
L16 761 S L13 AND (HIV OR AIDS OR IMMUNODEFICIENCY)  
L17 70 S L16 AND ((MURINE OR MOUSE) (A) CELL OR A20)  
L18 35 S L17 NOT PY>1997  
L19 8 DUP REM L18 (27 DUPLICATES REMOVED)  
L20 4 S L19 NOT (L6 OR L8)

L9 ANSWER 1 OF 3 MEDLINE on STN  
AN 97113334 MEDLINE  
DN 97113334 PubMed ID: 8955194  
TI Cloning of the **mouse fusin gene**, homologue  
to a human HIV-1 co-factor.  
AU Heesen M; Berman M A; Benson J D; Gerard C; Dorf M E  
CS Department of Pathology, Harvard Medical School, Boston, MA 02115, USA.  
NC CA67416 (NCI)  
NS31152 (NINDS)  
SO JOURNAL OF IMMUNOLOGY, (1996 Dec 15) 157 (12) 5455-60.  
Journal code: 2985117R. ISSN: 0022-1767.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals; AIDS  
OS GENBANK-U65580  
EM 199701  
ED Entered STN: 19970219  
Last Updated on STN: 19980206  
Entered Medline: 19970123  
AB Previous studies have demonstrated that **mouse** cells do not  
become infected with HIV-1 despite transfection with human **CD4**.  
Recently, a human protein termed "**fusin**" with characteristics of  
a seven-transmembrane-spanning **receptor** was found to be a  
co-factor required for the entry and fusion of HIV-1 with human  
**CD4**-bearing lymphocytes. Thus, cloning of the **murine**  
homologue of the human **fusin** (also termed **CXCR-4**)  
gene could provide an important comparative tool for  
identification of the structures crucial for **fusin** function.  
Using degenerate PCR, the **mouse** homologue of human **fusin**  
was cloned from a peritoneal exudate cell cDNA library. The predicted  
amino acid sequence is 91% identical to human **fusin**.  
Twenty-eight of the 37 amino acid differences between **mouse** and  
human **fusin** are located in the ectodomains, suggesting that the  
intracytoplasmic components that mediate G protein binding and signaling  
are highly conserved. Northern blot analysis showed a message of 2.2 kb  
in thymus, spleen, neutrophils, and primary astrocyte cultures. Lymphoid  
and monocyte cell lines also expressed message for **fusin**. The  
coding regions of most chemokine **receptors** lack introns. In  
contrast, cloning of genomic DNA for **mouse**  
**fusin** revealed the presence of a 2.3-Kb intron separating the  
first seven amino acids from the remaining 352 residues. Therefore, the  
**mouse fusin gene** has a unique genomic  
organization compared with other chemokine **receptors**.

L9 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN  
AN 1997:534140 CAPLUS  
DN 127:246942  
TI Two **murine** homologues of the human chemokine receptor  
**CXCR4** mediating stromal cell-derived factor 1.alpha. activation of  
Gi2 are differentially expressed in vivo  
AU Moepps, Barbara; Frodl, Reinhard; Rodewald, Hans Reimer; Baggiolini,  
Marco; Gierschik, Peter  
CS Department Pharmacology Toxicology, University Ulm, Ulm, D-89081, Germany  
SO European Journal of Immunology (1997), 27(8), 2102-2112  
CODEN: EJIMAF; ISSN: 0014-2980  
PB Wiley-VCH  
DT Journal  
LA English  
AB Previous results have shown that pertussis toxin-sensitive Gi proteins are

likely to be involved in regulating the emigration of mature thymocytes from the thymus. A low stringency polymerase chain reaction (PCR) approach was used to identify Gi protein-coupled cell surface **receptors** expressed in **mouse** thymocytes. Among the 10 G protein-coupled **receptor** cDNA isolated, the most prevalent cDNA encoded a polypeptide highly homologous to the human leukocyte-expressed 7-transmembrane-domain **receptor** LESTR, also referred to as HIV entry cofactor, **fusin**, or **CXCR4**. Isolation of full-length cDNA revealed that alternative RNA splicing produces transcripts encoding 2 isoforms of the **murine** LESTR, differing by the presence of 2 amino acids in the N-terminal portion of the longer protein. Functional reconstitution of recombinant **murine** LESTR with recombinant heterotrimeric G proteins in baculovirus-infected insect cells showed that both **receptor** variants mediate stromal cell-derived factor 1a activation of the pertussis toxin-sensitive G protein Gi2. **Receptor** subtype-specific reverse transcriptase-PCR anal. revealed differential expression of the 2 **receptor** mRNA in lymphoid tissues and brain, indicating that distinct functions are mediated by the 2 **receptor** isoforms in these tissues. The presence of LESTR mRNA in very early thymocytes as well as in immature (**CD4+** **CD8+**) thymocytes suggests that both **CD4** and LESTR are co-expressed and render developing human thymocytes susceptible for HIV entry, which may affect generation of both **CD4+** **CD8-** and **CD4-** **CD8+** mature lineages.

L9 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
AN 1997:440504 BIOSIS  
DN PREV199799739707  
TI **Murine CXCR-4** is a functional coreceptor for T-cell-tropic and dual-tropic strains of human immunodeficiency virus type 1.  
AU Bieniasz, Paul D.; Fridell, Robert A.; Anthony, Kara; Cullen, Bryan R. (1)  
CS (1) Box 3025, Duke Univ. Med. Cent., Durham, NC 27710 USA  
SO Journal of Virology, (1997) Vol. 71, No. 9, pp. 7097-7100.  
ISSN: 0022-538X.  
DT Article  
LA English  
AB The human chemokine **receptor** hCXCR-4 serves as a coreceptor for T-cell-tropic (T-tropic) and dual-tropic strains of human immunodeficiency virus type 1 (HIV-1). We have isolated a homolog of hCXCR-4 from a **murine** T-cell cDNA library and have examined its ability to function as an HIV-1 coreceptor. mCXCR-4 was found to be 91% identical to the human **receptor** at the amino acid level, with sequence differences concentrated in extracellular domains. Surprisingly, coexpression of both **hCD4** and mCXCR-4 on either simian or **murine** cell lines rendered them permissive for HIV-1-induced cell fusion, indicating that mCXCR-4 is a functional HIV-1 coreceptor. As with hCXCR-4, coreceptor function was restricted to T-tropic and dual-tropic HIV-1 strains. Ribonuclease protection analysis indicated that mCXCR-4 mRNA was expressed in only two of six **murine** cell lines tested. In contrast, Northern blot analysis of human and **mouse** tissues revealed that **CXCR-4** is widely expressed in both species *in vivo*. Overall, these data suggest that the reported lack of susceptibility of **hCD4+** **murine** cells to HIV-1 infection *in vitro* is, at least in part, due to a lack of mCXCR-4 expression rather than a lack of coreceptor function.

- L11 ANSWER 1 OF 20 MEDLINE on STN  
TI Angiogenic effects of prostaglandin E2 are mediated by up-regulation of CXCR4 on human microvascular endothelial cells.  
AU Salcedo Rosalba; Zhang Xia; Young Howard A; Michael Nelson; Wasserman Ken; Ma Wei-Hong; Martins-Green Manuela; Murphy William J; Oppenheim Joost J  
SO BLOOD, (2003 Sep 15) 102 (6) 1966-77.  
Journal code: 7603509. ISSN: 0006-4971.
- L11 ANSWER 2 OF 20 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN  
TI Expression of CXC chemokine receptor-4 enhances the pulmonary metastatic potential of **murine** B16 melanoma cells  
AU Murakami T.; Maki W.; Cardones A.R.; Fang H.; Tun Kyi A.; Nestle F.O.; Hwang S.T.  
SO Cancer Research, (15 DEC 2002), 62/24 (7328-7334), 34 reference(s)  
CODEN: CNREA8 ISSN: 0008-5472
- L11 ANSWER 3 OF 20 MEDLINE on STN  
TI Expression of the human CD4 receptor is sufficient for the transduction of murine T-cells with MLV/HIV pseudotyped vectors.  
AU Mitnacht-Kraus Rita; Schnierle Barbara S  
SO VIRUS RESEARCH, (2002 Aug) 87 (2) 129-34.  
Journal code: 8410979. ISSN: 0168-1702.
- L11 ANSWER 4 OF 20 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
TI Involvement of SDF-1/**CXCR4** interactions in the migration of immature human CD34+ cells into the liver of transplanted NOD/SCID mice.  
AU Kollet, Orit (1); Spiegel, Asaf (1); Dar, Ayelet (1); Samira, Sarit (1); Chen, Yuan-Qing; Shafritz, David A.; Suriawinata, Jenny; Thung, Swan; Seis-Dedos, Fernando Aranzena; Nagler, Arnon; Revel, Michel (1); Lapidot, Tsvee (1)  
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 549a.  
<http://www.bloodjournal.org/>. print.  
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001  
ISSN: 0006-4971.
- L11 ANSWER 5 OF 20 MEDLINE on STN  
TI TNF-alpha down-regulates **CXCR4** expression in primary **murine** astrocytes.  
AU Han Y; Wang J; He T; Ransohoff R M  
SO BRAIN RESEARCH, (2001 Jan 5) 888 (1) 1-10.  
Journal code: 0045503. ISSN: 0006-8993.
- L11 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN  
TI Leukotriene binding, signaling, and analysis of HIV coreceptor function in mouse and human leukotriene B4 receptor-transfected cells  
AU Martin, Viviane; Ronde, Philippe; Unett, David; Wong, Angela; Hoffman, Trevor L.; Edinger, Aimee L.; Doms, Robert W.; Funk, Colin D.  
SO Journal of Biological Chemistry (1999), 274(13), 8597-8603  
CODEN: JBCHA3; ISSN: 0021-9258
- L11 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN  
TI Transgenic **mouse** expressing human CD4 and **fusin** (**CXCR4**)  
IN Sawada, Shinichiro  
SO PCT Int. Appl., 33 pp.  
CODEN: PIXXD2
- L11 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN

- TI Chemokine, hematopoiesis, and development  
AU Nagasawa, Takashi  
SO Ensho to Men'eki (1998), 6(4), 425-430  
CODEN: ENMEFA; ISSN: 0918-8371
- L11 ANSWER 9 OF 20 MEDLINE on STN  
TI Identification of CCR8, the receptor for the human CC chemokine I-309.  
AU Roos R S; Loetscher M; Legler D F; Clark-Lewis I; Baggiolini M; Moser B  
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Jul 11) 272 (28) 17251-4.  
Journal code: 2985121R. ISSN: 0021-9258.
- L11 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN  
TI Shared usage of the chemokine receptor CXCR4 by the feline and human  
immunodeficiency viruses  
AU Willett, Brian J.; Picard, Laurent; Hosie, Margaret J.; Turner, Julie D.;  
Adema, Karen; Clapham, Paul R.  
SO Journal of Virology (1997), 71(9), 6407-6415  
CODEN: JOVIAM; ISSN: 0022-538X
- L11 ANSWER 11 OF 20 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN  
TI Role of the first and third extracellular domains of **CXCR-4** in human immunodeficiency virus coreceptor activity  
AU Brelo A.; Heveker N.; Pleskoff O.; Sol N.; Alizon M.  
SO Journal of Virology, (1997), 71/6 (4744-4751), 44 reference(s)  
CODEN: JOVIAM ISSN: 0022-538X
- L11 ANSWER 12 OF 20 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN  
TI STRL33, a novel chemokine **receptor**-like protein, functions as a  
fusion cofactor for both macrophage-tropic and T cell line-tropic HIV-1  
AU Liao F.; Alkhatib G.; Peden K.W.C.; Sharma G.; Berger E.A.; Farber J.M.  
SO Journal of Experimental Medicine, (1997), 185/11 (2015-2023), 41  
reference(s)  
CODEN: JEMEAV ISSN: 0022-1007
- L11 ANSWER 13 OF 20 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN  
TI Inhibition of human immunodeficiency virus fusion by a monoclonal  
antibody to a coreceptor (**CXCR4**) is both cell type and virus  
strain dependent  
AU McKnight A.; Wilkinson D.; Simmons G.; Talbot S.; Picard L.; Ahuja M.;  
Marsh M.; Hoxie J.A.; Clapham P.R.  
SO Journal of Virology, (1997), 71/2 (1692-1696), 34 reference(s)  
CODEN: JOVIAM ISSN: 0022-538X
- L11 ANSWER 14 OF 20 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN  
TI Expression cloning of new **receptors** used by simian and human  
immunodeficiency viruses  
AU Deng H.; Unutmaz D.; KewalRamani V.N.; Littman D.R.  
SO Nature, (1997), 388/6639 (296-300), 31 reference(s)  
CODEN: NATUAS ISSN: 0028-0836
- L11 ANSWER 15 OF 20 MEDLINE on STN  
TI The role of topoisomerase I in HIV-1 replication.  
AU Takahashi H; Tatsumi M; Matsuda M; Nagashima K; Kurata T; Hall W W  
SO LEUKEMIA, (1997 Apr) 11 Suppl 3 113-5.  
Journal code: 8704895. ISSN: 0887-6924.
- L11 ANSWER 16 OF 20 MEDLINE on STN  
TI The role of topoisomerase I in HIV-1 replication.  
AU Takahashi H; Tatsumi M; Matsuda M; Nagashima K; Kurata T; Hall W W  
SO LEUKEMIA, (1997 Apr) 11 Suppl 3 26-8.  
Journal code: 8704895. ISSN: 0887-6924.

- L11 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2003 ACS on STN  
TI Molecular cloning and characterization of a **murine** pre-B-cell growth-stimulating factor/stromal cell-derived factor 1 receptor, a **murine** homolog of the human immunodeficiency virus 1 entry coreceptor **fusin**  
AU Nagasawa, Takashi; Nakajima, Toshihiro; Tachibana, Kazunobu; Iizasa, Hisashi; Bleul, Conrad C.; Yoshie, Osamu; Matsushima, Kouji; Yoshida, Nobuaki; Springer, Timothy A.; Kishimoto, Tadamitsu  
SO Proceedings of the National Academy of Sciences of the United States of America (1996), 93(25), 14726-14729  
CODEN: PNASA6; ISSN: 0027-8424
- L11 ANSWER 18 OF 20 LIFESCI COPYRIGHT 2003 CSA on STN  
TI Fusin - A place for HIV-1 and T4 cells to meet  
AU Dimitrov, D.S.  
SO NAT. MED., (1996) vol. 2, no. 6, pp. 640-641.  
ISSN: 1078-8956.
- L11 ANSWER 19 OF 20 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN  
TI Human immunodeficiency virus type-1 susceptible whole cell and microcell hybrids  
AU Harrington R.D.; Geballe A.P.  
SO Annals of Clinical and Laboratory Science, (1996), 26/6 (522-530)  
CODEN: ACLSCP ISSN: 0091-7370
- L11 ANSWER 20 OF 20 BIOTECHNO COPYRIGHT 2003 Elsevier Science B.V. on STN  
TI **CD4**-induced interaction of primary HIV-1 gp120 glycoproteins with the chemokine **receptor** CCR-5  
AU Wu L.; Gerard N.P.; Wyatt R.; Choe H.; Parolin C.; Ruffing N.; Borsetti A.; Cardoso A.A.; Desjardin E.; Newman W.; Gerard C.; Sodroski J.  
SO Nature, (1996), 384/6605 (179-183)  
CODEN: NATUAS ISSN: 0028-0836

L8 ANSWER 3 OF 12 MEDLINE on STN DUPLICATE 1  
AN 2002435120 MEDLINE  
DN 22180309 PubMed ID: 12191776  
TI Expression of the human CD4 receptor is sufficient for the transduction of murine T-cells with MLV/HIV pseudotyped vectors.  
AU Mitnacht-Kraus Rita; Schnierle Barbara S  
CS Georg-Speyer-Haus, Institute for Biomedical Research, Paul-Ehrlich-Strasse 42-44, D-60596 Frankfurt/Main, Germany.  
SO VIRUS RESEARCH, (2002 Aug) 87 (2) 129-34.  
Journal code: 8410979. ISSN: 0168-1702.  
CY Netherlands  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 200211  
ED Entered STN: 20020823  
Last Updated on STN: 20021212  
Entered Medline: 20021120  
AB **Murine** leukemia virus (MLV) can be pseudotyped with a variant of the HIV envelope **gene** encoding the surface glycoprotein gp120-SU and a carboxyl-terminally truncated transmembrane (TM) protein, with only seven cytoplasmic amino acids. MLV/HIV pseudotyped retroviral vectors selectively target human CD4+ cells and can be used as tools to study entry of HIV into cells. **Mouse** T-cells are immune to HIV infection, which is primarily caused by the weak binding affinity of HIV gp120 to the **murine** CD4 receptor. Here we show that expression of the human CD4 receptor in **murine** T-cells is sufficient for syncytia formation with HIV-1 envelope expressing cells and entry of MLV/HIV pseudotyped retroviral vectors. This implies that the **murine CXCR4** receptor is a functional coreceptor for MLV/HIV pseudotyped vectors and confirms previous data that the inability of HIV to replicate in **murine** T-cells is due to a post entry block.

L8 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN  
AN 2002:199000 BIOSIS  
DN PREV200200199000  
TI Involvement of SDF-1/**CXCR4** interactions in the migration of immature human CD34+ cells into the liver of transplanted NOD/SCID **mice**.  
AU Kollet, Orit (1); Spiegel, Asaf (1); Dar, Ayelet (1); Samira, Sarit (1); Chen, Yuan-Qing; Shafritz, David A.; Suriawinata, Jenny; Thung, Swan; Seis-Dedos, Fernando Aranzena; Nagler, Arnon; Revel, Michel (1); Lapidot, Tsvee (1)  
CS (1) Immunology, Weizmann, Rehovot Israel  
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 549a.  
<http://www.bloodjournal.org/>. print.  
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001  
ISSN: 0006-4971.  
DT Conference  
LA English  
AB Recent studies have demonstrated the potential of hematopoietic stem cells to migrate to the liver, differentiate, and give rise to functional hepatocytes in both human and **murine** transplanted recipients. The chemokine SDF-1, a powerful chemoattractant for immature and mature hematopoietic cells, is widely expressed in many tissues and organs, including the **murine** liver and also by epithelial cells within the fetal human liver. We previously established a crucial role for SDF-1/**CXCR4** interactions in mediating human stem cell homing and

repopulation in transplanted immune deficient NOD/SCID and NOD/SCID/B2mnull **mice**. In addition, preliminary results reveal that SDF-1/**CXCR4** interactions also play a major role in human and **murine** G-CSF induced stem and progenitor cell mobilization. In the current study, we determined the levels of human/**mouse** chimerism within the liver of **mice** 5-7 weeks post transplantation of immature human CB CD34+ cells, and the role of **CXCR4** in migration of human progenitor cells to the liver of these **mice**. Our results demonstrate low levels of human **DNA** detected in the liver of engrafted **mice** (0.1%-0.8%). These findings suggest limited potential of human progenitor cells to migrate or to be retained within the **murine** liver, or alternatively poor proliferative support provided by the **murine** liver for human progenitors. Interestingly, when CB CD34+ transplanted cells were pretreated with the neutralizing anti human **CXCR4** mAb (clone 12G5), human **DNA** could not be detected in the liver of engrafted **mice**, demonstrating that **CXCR4** is also involved in migration of human cells to the **murine** liver. Moreover, anti **CXCR4** Ab pre-treatment of human CD34+ cells from mobilized PBL, significantly reduced (70% inhibition) the levels of human progenitors homing to the **murine** liver 16hr. post transplantation. By immunohistochemical staining of **mouse** liver, we show SDF-1 expression in the fetal liver, including endothelium of d16 embryos, while in the adult liver SDF-1 is expressed exclusively by epithelial cells of the bile ducts, which are in close proximity to the portal veins. Interestingly, we also found SDF-1 in the adult human liver in bile ducts, bile ductules (where liver stem cells are thought to be located) and also in some endothelial cells. The cytokine TNF has been shown to induce priming of the **murine** liver by sensitizing hepatocytes to proliferate in response to growth factors. Recently, we showed that TNF induced human T cell development in transplanted NOD/SCID **mice**. Present results show enhanced levels of human **DNA** in the liver of some **mice** pretreated with TNF and transplanted with human MNC (up to 10%-20%) compared to control **mice** (generally in the range of 0.1%-3%), suggesting that TNF affects also the level of human hematopoietic cells in the **murine** liver. The ability of human hematopoietic cells to differentiate into hepatic epithelial cells within the **murine** liver and the role of SDF-1 produced by the bile duct epithelium in this process are currently under study. Our findings show a major role for SDF-1/**CXCR4** in migration of human progenitor cells to the liver of transplanted **mice**.

L8 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1998:712336 CAPLUS

DN 129:311707

TI Transgenic **mouse** expressing human CD4 and **fusin** (**CXCR4**)

IN Sawada, Shinichiro

PA Japan Science and Technology Corp., Japan

SO PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9846734	A1	19981022	WO 1998-JP1767	19980417
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,			

NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,  
 UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
 CM, GA, GN, ML, MR, NE, SN, TD, TG  
 US 6255555 B1 20010703 US 1998-61048 19980416  
 AU 9868532 A1 19981111 AU 1998-68532 19980417  
 EP 975746 A1 20000202 EP 1998-914068 19980417  
 R: DE, FR, GB  
 JP 2000513584 T2 20001017 JP 1998-543750 19980417  
 PRAI JP 1997-100615 A 19970417  
 WO 1998-JP1767 W 19980417

AB This invention provides a transgenic **mouse** capable of expressing at least two cell surface membrane proteins of human T lymphocytes, transgenes for use in prodn. of the transgenic **mouse**, and a method for producing the transgenic **mouse** using the transgenes. The cell surface membrane proteins of human T lymphocytes are assocd. particularly with human immunodeficiency virus (HIV) infection, and are preferably human CD4 and **fusin (CXCR4)**. The transgenic **mouse** is able to transmit to its progeny a trait for expression of the cell surface membrane proteins of human T lymphocytes, thus being useful for an animal model for HIV infection and AIDS. One construct was prep'd. with human **CXCR4** fused to a **murine CD4 gene** contg. enhancer, promoter, and silencer elements as well as a SV40 polyadenylation signal. Another construct contained the human CD4 **gene** with **murine CD4 enhancer**. Transgenic **mice** were produced by introducing both constructs into fertilized eggs by microinjection. Human CD4 and **fusin** were expressed on **murine CD4+ T lymphocytes**.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1998:406366 CAPLUS  
 DN 129:80274  
 TI Chemokine, hematopoiesis, and development  
 AU Nagasawa, Takashi  
 CS Res. Lab., Osaka Med. Cent. Matern. Child Health, Izumi, 590-02, Japan  
 SO Ensho to Men'eki (1998), 6(4), 425-430  
 CODEN: ENMEFA; ISSN: 0918-8371  
 PB Sentan Igakusha  
 DT Journal; General Review  
 LA Japanese  
 AB A review with 17 refs. This review focuses on characterization of stromal cell-derived factor-1/ pre-B-cell growth stimulating factor (SDF-1/PBSF). Expression of the SDF-1/PBSF **gene** has been discussed. Physiol. function of SDF-1/PBSF has been describes including the data from the studies using SDF-1/PBSF-deficient **mice**. Furthermore, identification of SDF-1/PBSF receptor, **CXCR4** as a **murine homolog** of the human immunodeficiency virus 1 entry coreceptor, **fusin**, has also been reviewed. Finally, the significance of **CXCR4** being a **murine homolog** of **fusin**, has been discussed.

L8 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2003 ACS on STN  
 AN 1997:534140 CAPLUS  
 DN 127:246942  
 TI Two **murine homologues** of the human chemokine receptor **CXCR4** mediating stromal cell-derived factor 1.alpha. activation of Gi2 are differentially expressed in vivo

AU Moepps, Barbara; Frodl, Reinhard; Rodewald, Hans Reimer; Baggioolini, Marco; Gierschik, Peter  
CS Department Pharmacology Toxicology, University Ulm, Ulm, D-89081, Germany  
SO European Journal of Immunology (1997), 27(8), 2102-2112  
CODEN: EJIMAF; ISSN: 0014-2980

PB Wiley-VCH

DT Journal

LA English

AB Previous results have shown that pertussis toxin-sensitive Gi proteins are likely to be involved in regulating the emigration of mature thymocytes from the thymus. A low stringency polymerase chain reaction (PCR) approach was used to identify Gi protein-coupled cell surface receptors expressed in **mouse** thymocytes. Among the 10 G protein-coupled receptor cDNA isolated, the most prevalent cDNA encoded a polypeptide highly homologous to the human leukocyte-expressed 7-transmembrane-domain receptor LESTR, also referred to as HIV entry cofactor, **fusin**, or **CXCR4**. Isolation of full-length cDNA revealed that alternative RNA splicing produces transcripts encoding 2 isoforms of the **murine** LESTR, differing by the presence of 2 amino acids in the N-terminal portion of the longer protein. Functional reconstitution of recombinant **murine** LESTR with recombinant heterotrimeric G proteins in baculovirus-infected insect cells showed that both receptor variants mediate stromal cell-derived factor 1a activation of the pertussis toxin-sensitive G protein Gi2. Receptor subtype-specific reverse transcriptase-PCR anal. revealed differential expression of the 2 receptor mRNA in lymphoid tissues and brain, indicating that distinct functions are mediated by the 2 receptor isoforms in these tissues. The presence of LESTR mRNA in very early thymocytes as well as in immature (CD4+ CD8+) thymocytes suggests that both CD4 and LESTR are co-expressed and render developing human thymocytes susceptible for HIV entry, which may affect generation of both CD4+ CD8- and CD4- CD8+ mature lineages.

L20 ANSWER 1 OF 4 MEDLINE on STN  
AN 2001280096 MEDLINE  
DN 96701560 PubMed ID: 11363488  
TI NIH scientists find cofactor for **HIV** entry. National Institutes of Health.  
AU James J S  
SO AIDS TREATMENT NEWS, (1996 May 17) (no 247) 1, 6.  
Journal code: 8809835. ISSN: 1052-4207.  
CY United States  
DT (NEWSPAPER ARTICLE)  
LA English  
FS AIDS  
EM 199607  
ED Entered STN: 20010529  
Last Updated on STN: 20020222  
Entered Medline: 19960701  
AB The discovery of a **fusin** protein by researchers at the National Institute of Allergy and Infectious Diseases (NIAID) is considered to be a major advance in the understanding of how **HIV** disease develops. The discovery does not seem to have immediate implications for treatment. **Fusin** works together with the CD4 protein to allow **HIV** to fuse with and enter CD4 cells (T-helper cells). The research was initiated with laboratory **mice**. **Mouse cells** were changed genetically so that they would express a human CD4. **Fusin** exists naturally in human cells and is thought to have a normal function, although this function is yet unknown.

L20 ANSWER 2 OF 4 MEDLINE on STN  
AN 1998001346 MEDLINE  
DN 98001346 PubMed ID: 9343181  
TI Neutralizing antibodies against the V3 loop of human **immunodeficiency** virus type 1 gp120 block the CD4-dependent and -independent binding of virus to cells.  
AU Valenzuela A; Blanco J; Krust B; Franco R; Hovanessian A G  
CS Unite de Virologie et d'Immunologie Cellulaire, Institut Pasteur, Paris, France.  
SO JOURNAL OF VIROLOGY, (1997 Nov) 71 (11) 8289-98.  
Journal code: 0113724. ISSN: 0022-538X.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; AIDS  
EM 199711  
ED Entered STN: 19971224  
Last Updated on STN: 19971224  
Entered Medline: 19971113  
AB The CD4 molecule is an essential receptor for human **immunodeficiency** virus type 1 (**HIV-1**) through high-affinity interactions with the viral external envelope glycoprotein gp120. Previously, neutralizing monoclonal antibodies (MAbs) specific to the third hypervariable domain of gp120 (the V3 loop) have been thought to block **HIV** infection without affecting the binding of **HIV** particles to CD4-expressing human cells. However, here we demonstrate that this conclusion was not correct and was due to the use of soluble gp120 instead of **HIV** particles. Indeed, neutralizing anti-V3 loop MAbs inhibited completely the binding and entry of **HIV** particles into CD4+ human cells. In contrast, the binding of virus was only partially inhibited by neutralizing anti-CD4 MAbs against the gp120 binding site in CD4, which, like the anti-V3 loop MAbs, completely inhibited **HIV** entry and infection. Nonneutralizing control MAbs

against either the V3 loop or the N or C terminus of gp120 had no significant effect on **HIV** binding and entry. **HIV-1** particles were also found to bind human and **murine cells** expressing or not expressing the human CD4 molecule. Interestingly, the binding of **HIV** to CD4+ **murine cells** was inhibited by both anti-V3 and anti-CD4 MAbs, whereas the binding to human and **murine** CD4- cells was affected only by anti-V3 loop MAbs. The effect of anti-V3 loop neutralizing MAbs on the **HIV** binding to cells appears not to be the direct consequence of gp120 shedding from **HIV** particles or of a decreased affinity of CD4 or gp120 for binding to its surface counterpart. Taken together, our results suggest the existence of CD4-dependent and -independent binding events involved in the attachment of **HIV** particles to cells; in both of these events, the V3 loop plays a critical role. As **murine** cells lack the specific cofactor **CXCR4** for **HIV**-1 entry, other cell surface molecules besides CD4 might be implicated in stable binding of **HIV** particles to cells.

L20 ANSWER 3 OF 4 MEDLINE on STN  
AN 97404731 MEDLINE  
DN 97404731 PubMed ID: 9261443  
TI **Murine CXCR-4** is a functional coreceptor for T-cell-tropic and dual-tropic strains of human **immunodeficiency** virus type 1.  
AU Bieniasz P D; Fridell R A; Anthony K; Cullen B R  
CS Howard Hughes Medical Institute, Duke University Medical Center, Durham, North Carolina 27710, USA.  
SO JOURNAL OF VIROLOGY, (1997 Sep) 71 (9) 7097-100.  
Journal code: 0113724. ISSN: 0022-538X.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; AIDS  
EM 199709  
ED Entered STN: 19970926  
Last Updated on STN: 19980206  
Entered Medline: 19970917  
AB The human chemokine receptor hCXCR-4 serves as a coreceptor for T-cell-tropic (T-tropic) and dual-tropic strains of human **immunodeficiency** virus type 1 (**HIV-1**). We have isolated a homolog of hCXCR-4 from a **murine** T-cell cDNA library and have examined its ability to function as an **HIV-1** coreceptor. mCXCR-4 was found to be 91% identical to the human receptor at the amino acid level, with sequence differences concentrated in extracellular domains. Surprisingly, coexpression of both hCD4 and mCXCR-4 on either simian or **murine** cell lines rendered them permissive for **HIV-1**-induced cell fusion, indicating that mCXCR-4 is a functional **HIV-1** coreceptor. As with hCXCR-4, coreceptor function was restricted to T-tropic and dual-tropic **HIV-1** strains. Ribonuclease protection analysis indicated that mCXCR-4 mRNA was expressed in only two of six **murine** cell lines tested. In contrast, Northern blot analysis of human and **mouse** tissues revealed that **CXCR-4** is widely expressed in both species in vivo. Overall, these data suggest that the reported lack of susceptibility of hCD4+ **murine** cells to **HIV**-1 infection in vitro is, at least in part, due to a lack of mCXCR-4 expression rather than a lack of coreceptor function.

L20 ANSWER 4 OF 4 MEDLINE on STN  
AN 97296517 MEDLINE  
DN 97296517 PubMed ID: 9151712

TI **CXCR4/fusin** is not a species-specific barrier in  
**murine cells** for **HIV-1** entry.

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Yoshie O; Kishimoto T; Nagasawa T

CS Department of Immunology, Research Institute, Osaka Medical Center for  
Maternal and Child Health, Osaka 590-02, Japan.

SO JOURNAL OF EXPERIMENTAL MEDICINE, (1997 May 19) 185 (10) 1865-70.  
Journal code: 2985109R. ISSN: 0022-1007.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals; AIDS

EM 199706

ED Entered STN: 19970709  
Last Updated on STN: 20000303  
Entered Medline: 19970624

AB Since some **murine cells** expressing human CD4 fail to internalize **HIV-1**, another block was thought to be located at the level of viral entry in addition to CD4. Recently, **CXCR4** was shown to function as a coreceptor for T cell line-tropic **HIV-1** entry. Here we demonstrated that cells expressing **murine CXCR4** and human CD4 fused with cells expressing the env proteins derived from T cell line-tropic **HIV-1** and were infected with T cell line-tropic **HIV-1** strains. In contrast, the same cells were not infected with chimeric clones constructed by substitution of monocyte- or macrophage-tropic strain-derived env region or V3 region into T cell line-tropic **HIV-1**, indicating V3 loop of envelope protein is required for **murine CXCR4**mediated **HIV-1** entry. We conclude that **murine CXCR4** is not a species specific barrier to the entry of T cell line-tropic **HIV-1**.